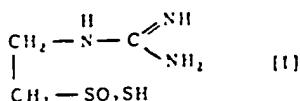


B1

87-140943/20 SOUGO YAKKOU KK	B05 02.10.85 *J6 2081-365-A 02.10.85-JP-218009 (14.04.87) A61k-31/18 C07c-161	Guonidino ethane thiosulphonic acid cholesterol decreasing agent - prep. by reacting guonidino ethane sulphonic acid with sulphur in presence of base C87-058856
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Guonidinoethanethiosulphonic acid of formula [I] is new:



USE/ADVANTAGE

[I] is useful as cholesterol decreasing agent. The compound has strong cholesterol decreasing activity and strong HDL-cholesterol increasing activity without toxicity ($\text{LD}_{50} = 3000 \text{ mg/Kg}$ in the rat).

PREPARATION

Cpd. [I] is prepared by reacting hypotaurocyanine (guonidinoethanesulphonic acid) with sulphur in the presence

B(10-A9B, 12-G1A, 12-H3) 3

B017C

of base.

Caustic alkali such as NaOH, KOH is used as base. Powdered sulphur is pref. used.

Solvent is pref. an alcohol such as MeOH, EtOH or i-PrOH.

ACTIVITY

Test results on male rats allowed to eat normal food, cholesterol food, and cholesterol food with [I] (200 mg/Kg/day) for 2 weeks [total] cholesterol in serum, HDL-cholesterol in serum, HDL-cholesterol (mg/dl) are: 109.2, 48.2, 521.2, 20.5; 263.9, 28.1.

EXAMPLE

Hypotaurocyanine (0.18 mol) was dissolved in 0.2N NaOH. EtOH (1800 ml) and sulphur (6.3g) were added. The mixture was stirred under reflux until the sulphur completely disappeared and was allowed to stand overnight. Crude crystals were filtered and washed with CS₂ (twice) and EtOH. The crystals were dissolved in hot water and recrystallized by adding EtOH (2700ml) and cooling. Filtration and washing with ether afforded 26.4 g (80.1%) of [I]. mp 206-210°C. (SppW67EDDwgNo0/0).
J62081365-A

87-140944/20 TOHYOH STAUFER CHEM	B03 02.10.85-JP-219681 (14.04.87) C07d-205/08	TOST-02.10.85 *J6 2081-368-A
Highly stereoselective synthesis of beta-lactam deriv. - by treating lithium enolate of organic ester with organic imine cpd. in polar solvent C87-058857		

B-Lactam derivs. are synthesized highly selectively by treating lithium enolate of organic ester with organic imine cpd. in polar solvent.

The organic imine cpd. may be an imine coordinated with trialkylaluminum. When the cpd. is used as imine, cis prod. may be synthesized with 100% stereoselectivity.

USE/ADVANTAGE

Lactams are formed with high stereoselectivity. Prods. are useful as pharmaceuticals.

EXAMPLE

n-BuLi (15% hexane soln.) (12 m mols.) was added to a soln. of diisopropylamine (12 m mols.) in n-hexane (7 ml) with ice-cooling under N₂, and resultant mixt. was stirred. n-Hexane was distilled off under reduced press.. THF (5 ml) was added to the residue, and the mixt. was cooled to -78°C.

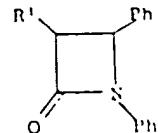
B(7-D1) 1

B0171

(C₂H₅)₂ClCH₂COOC₂H₅ or C₂H₅ClCH₂COOC₂H₅ (10 m mols) was added within three minutes to the above mixt., and a soln. of C₆H₅CH=NC₂H₅ (10 m mols) in THF (5 ml) or a soln. of the imine (10 m mols) and AlR₃ (see below), (10 mmols) in THF (5 m mols) was added.

The low temp. cooling bath was removed and temp. of reaction mixt. was elevated slowly to room temp. over ten hours. The mixt. was then hydrolysed with 1N HCl aq. soln. and prod. was extracted with benzene to give B-lactam.

Yield of the B-lactam and results of cis : trans ratio are as follows:



(a) R¹ = i-Pr:

J62081368-A

AIR ₃	Yield (%)	Cis : trans ratio
None	87	0 : 100
Al(C ₂ H ₅) ₃	73	100 : 0
Al(C ₂ H ₅) ₂	75	100 : 0
Ali-Bu ₃	40	100 : 0

(b) R = ClC₂H₅:

AIR ₃	Yield (%)	Cis : trans ratio
None	92	0 : 100
Al(C ₂ H ₅) ₃	85	100 : 0
Al(C ₂ H ₅) ₂	83	100 : 0
Ali-Bu ₃	52	100 : 0

(SppW69EDDwgNo0/0).

J62081368-A